Opposing activities of Notch and Wnt signaling regulate intestinal stem cells and gut homeostasis.

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Public Summary:
Proper organ homeostasis requires tight control of adult stem cells and differentiation through the integration of multiple inputs. In the mouse small intestine, Notch and Wnt signaling are required both for stem cell maintenance and for a proper balance of differentiation between secretory and absorptive cell lineages. In the absence of Notch signaling, stem cells preferentially generate secretory cells at the expense of absorptive cells. Here, we use function-blocking antibodies against Notch receptors to demonstrate that Notch blockade perturbs intestinal stem cell function by causing a derepression of the Wnt signaling pathway, leading to misexpression of prosecretory genes. Importantly, attenuation of the Wnt pathway rescued the phenotype associated with Notch blockade. These studies bring to light a negative regulatory mechanism that maintains stem cell activity and balanced differentiation, and we propose that the interaction between Wnt and Notch signaling described here represents a common theme in adult stem cell biology.

Scientific Abstract:
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